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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,771	04/07/2005	Louis Casteilla	SERVIER 450 PCT	4717

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EXAMINER	
RAO, SAVITHA M	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,771	CASTEILLA ET AL.	
	Examiner	Art Unit	
	SAVITHA RAO	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26 and 32-44* is/are pending in the application.

4a) Of the above claim(s) *33-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26, 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 26 and 32-44 are pending.

Receipt and consideration of Applicants' amended claim set and remarks/arguments mailed on 09/14/2009 is acknowledged. Claims 27-31 were cancelled and claim 26 was amended. Claims 33-44 are withdrawn from consideration as being drawn to a non-elected invention. Claims under consideration in the instant office action are claims 26 and 32

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/14/2009 has been entered.

Applicants' arguments, filed 09/14/2009 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 26 and dependent claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

. Claim 26 is vague and indefinite in that the recitation of "comprising a combination of coenzyme Q10 and rosiglitazone or an addition salt thereof with a pharmaceutically acceptable acid or base" in the penultimate and last line of the claim is unclear, because it is not clearly understood whether that phrase indicates a combination of coenzyme Q10 and rosiglitazone and/or a combination of coenzyme Q10 with an addition salt of rosiglitazone or does it indicate a combination of an addition salt of coenzyme Q10 with rosiglitazone.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Rejection of instant claims 26 and 32 under 35 U.S.C. 103(a) as being unpatentable over Watts et al (WO 02/34259) is being maintained for reasons of record restated below.

Watts disclose a composition comprising a peroxisome proliferator activated receptor (PPAR) activator and a benzoquinone (abstract and page 3, lines 6-8, Claim 1). Watts disclose that the PPAR activator preferred is a fibrate or a thiazolidinedione, more preferably fenofibrate (page 4, lines 14-17). In claim 10, page 26, Watts recites that the PPAR activator in his composition of his claim 1 to be either PPARα or PPARγ. Furthermore, Watts teaches that PPAR activators are activators of PPARα or PPARγ and a number of activators are known in the art including the fibrate and thiazolidinedione classes of drugs, for which fenofibrate and rosiglitazone respectively

are well known examples. Watts teaches that the preferred benzoquinone or precursor thereof is a ubiquinone or precursor thereof, more preferably, coenzyme Q_{10} or a precursor thereof (page 4, line11-12, claim 4) and teaches that Benzoquinones used in his present invention should have antioxidant properties, such as the ability to scavenge active oxygen species (page 10, lines 11-13). Watts additionally teaches that *in vivo* the oxidized CoQ_{10} is converted to reduced $CoQ_{10}H_2$ or ubiquinal-10, a potent antioxidant in Plasma, in lipoproteins and in tissues (col. 11, lines 27-30). Finally, Watts teaches that his invention also provides a pharmaceutical composition comprising a composition of the invention together with a pharmaceutically acceptable carrier or diluent (col.4, lines 22-24, claim 8).

It is prima facie obvious to one of ordinary skill in the art to substitute rosiglitazone (specific PPARγ ligand) with fenofibrate (specific PPARα ligand) in combination with an antioxidant such as coenzyme Q_{10} taught by Watts et al. An ordinary skilled artisan would have been motivated to formulate such a composition comprising a combination of an antioxidant and rosliglitazone since a combination of PPAR ligand with an antioxidant has been previously taught in the art to be used for lowering triglycerides. Additionally, as taught by Watt's et al, different PPAR activators are known to exert similar physiological action with respect to lowering triglyceride level and substitution of one to another or inclusion of two such agents in a composition would be expected to elicit similar if not additive effect. Accordingly, one of ordinary skill in the art would have been imbued with a reasonable expectation of success based on the prior art that a composition comprising rosliglitazone and antioxidant for lowering

cholesterol and triglycerides to develop a more effective treatment option for conditions such as obesity and arthrosclerosis.

Response to Applicant's argument submitted on 09/14/2009

Applicant traverses the above rejection with the disclosure of unexpected data associated with their instantly claimed compositions submitted in the form of declaration submitted on 09/14/2009

With regards to the Applicant's argument of unexpected results, Applicants data presented in the instant disclosure (page 7-8) and the data presented in the affidavit 1.132 submitted on 09/14/2009 have been considered and although is persuasive, it has been found not be commensurate to the scope of the instant claim.

The data presented in the declaration of 09/14/2009 is partially persuasive. The data clearly shows the unexpected effect of the combination or rosliglitazone and Coenzyme Q10 in both the reduction of insulinemia and in the reduction of weight gain as demonstrated in Figure 1 and 2 of the declaration. In both these instances the testing protocol involved injection of the test compounds and once daily for 14 days (Protocol for insulinemia study) or for 7 days (for the obesity study as described in the 1.132 affidavit of 1/13/2009) in a specific carrier (5% DMSO/15% solutol/ heated to 65°C), additionally, the solution was pre-heated before injection in both instances. In addition in both the cited tests rosiglitazone was tested at a single concentration of 10 mg/kg and Coenzyme Q10 was also tested at the single concentration of 10 mg/kg. It is not clear

from the data presented that increasing or decreasing the concentrations of either of the two agent's rosliglitazone or Coenzyme Q10 would result in similar unexpected results.

As such, the exact concentration of the agents the process of administration, preheating of the solution before injection appears to be critical to achieve the data observed in the studies presented. The instant claims are claimed broadly to a composition comprising a combination of rosiglitazone with Coenzyme Q10 or an addition salt thereof with a pharmaceutically acceptable acid or base. For e.g. the unexpected results do not disclose data at a range of concentrations for the two agents where in the unexpected results are observed. There is not data to show that the same results are obtained with use of the addition salt with pharmaceutically acceptable acid or base of Coenzyme Q10 or addition salt with pharmaceutically acceptable acid or base of rosliglitazone. The instant claims do not recite the limitations in terms of the concentrations, method of administration etc, which are required to achieve the demonstrated synergistic effect. As such the data supplied is not in commensuration with the scope of the instant claims. Therefore, the unexpected results observed in these studies are with very specific parameters and are therefore not commensurate with the full scope of what is claimed and the data is not probative of nonobviousness of the full scope of the claims as discussed above,

Additionally, the instant claims are drawn to a composition comprising a combination of PPAR ligand and an antioxidant. The unexpected results as argued by the applicants are obtained with the method of use of the instantly claimed compositions. However, such compositions are known and were taught in the prior art

at the time of the invention as described by Watt et.al. As such the properties of the individual compounds in the compositions i.e. the PPAR ligand and antioxidant such as coenzyme Q10 would be inherently present in the composition. A compound and its characteristics cannot be separated. As such the functional properties of reducing weight gain when treated together would have been present in the composition of Watt which teaches a combination as instantly claimed. It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Accordingly, the above rejection is maintained.

Conclusion

Claims 26 and 32 are rejected. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 7 am to 4 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SAVITHA RAO/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614